REMARKS

This responds to the Final Office Action mailed on July 15, 2009.

Claims 24-27, 33-36, 38-39 and 40 have been canceled without prejudice and claim 41 has been added. As a result, claims 2, 4, 8, 9, 10, 28, 29, 30, 31, 32, 37 and 41 are now pending in this application.

Claim 41 recites that the antigenic peptide stimulates proliferation of cytotoxic T cells. Support for stimulation of T cell replication by the antigenic peptide is present throughout the specification as filed, for example, at page 8, lines 14-22; at page 9, lines 15-20.and at page 10, lines 21-26.

Claims 2 and 37 are amended. In particular, the subject matter of claims 39 and 40 has been inserted into claims 2 and 37, respectively. The term "cancer" has also been inserted into claim 37. Support for presentation of an antigen on a viable cancer cell is present throughout the specification as filed, for example, at page 9, lines 24-25, in Example 2, and in claim 2. The term "stimulate" is now used in claim 2 rather than "generate" so that the antigenic peptide, or a part thereof is of sufficient size to stimulate a cytotoxic T cell response. Support for stimulation of a T cell response is present throughout the specification as filed, for example, at page 9, lines 15-20 and at page 10, lines 21-26.

Applicants submit that no new matter has been added to the application.

§ 112, First Paragraph, Rejection of the Claims

Claims 2, 4, 8-10, 24-38, and newly added claims 39 and 40 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. According to the Examiner, there is no evidence of record showing the generation of a primary (naïve) MHC class I restricted immune response or a class II restricted immune response.

Although Applicants maintain that the claimed subject matter is clearly enabled by the specification, the subject matter relating to claims 39 and 40 has been incorporated into independent claims 2 and 37, respectively. Thus, claim 2 is directed to a method of presenting an antigenic peptide on the surface of a viable cancer cell wherein such presentation results in cytotoxic T cell mediated cell killing by a cytotoxic T cell specific to said antigenic peptide or a

part thereof. Claim 37 is directed to a method of presenting an antigenic peptide (or part thereof) on the surface of a viable cancer cell wherein presentation of the peptide (or part thereof) on the surface of said cell can stimulate in the patient cytotoxic T cell mediated cell killing by cytotoxic T cells specific to said antigenic peptide or a part thereof.

The claims embrace subject matter that is fully enabled by the specification and do not include subject matter that the Examiner alleges lack enablement. Thus, the claims refer to a cytotoxic T cell response mediated by cytotoxic T cells specific for the antigenic peptide, i.e. the cytotoxic T cells are already primed.

These methods are fully supported by the specification and illustrated by the experimental data shown in Example 2. As is known to one of skill in the art, and as described in the specification (page 8, lines 11-19), cytotoxic T cells specifically interact with antigenic peptides and T cells can also stimulate production of more cytotoxic T cells. The evidence of record clearly shows presentation of peptide antigens on the surface of cells subjected to the methods of the invention, and killing of those cells by cytotoxic T cells. In particular, Applicants have provided data explicitly showing that cell killing by cytotoxic T cells occurs only when the cytotoxic T cell recognizes a previously internalized antigenic peptide on the surface of a cancer cell (see Example 2). These data also demonstrate that methods of the invention achieve presentation of sufficient antigenic peptide to allow recognition and cytotoxic T cell-mediated cell killing of the cancer cells that internalized and presented the peptide on their cell surface (FIG. 3).

The Examiner asserts that a cancer cell, except for a transformed antigen presenting cell, would not be able to induce a primary immune response and states that there is no evidence of record to support generation of a class II MHC response. According to the Examiner, it is allegedly well-established that cytosolic antigens are processed and presented only through the MHC class I pathway and a cytotoxic T cell response allegedly cannot be generated by the methods of the invention.

Applicants submit that the recited result of claims 2 and 37 for cytotoxic T cell mediated cancer cell killing addresses the Examiner's concerns. The claims specifically recite that presentation of the antigenic peptide results in cytotoxic T cell mediated cell killing by a cytotoxic T cell specific to said antigenic peptide and are not concerned with generating a

primary immune response. Claims 2 and 37 also recite that presentation of the antigenic peptide on the surface of the cancer cell is "by a class I MHC molecule" and the term "generate" in claim 2 has been amended to "stimulate."

The element relating to cytotoxic T cell mediated cancer cell killing relates to the type of antigenic peptide employed in Applicants' methods. Many cancer antigens and cancer markers are known, against which cancer patients have memory T cells. One of skill in the art can readily select and employ a such a cancer antigen or marker and employ it as an antigenic peptide in Applicants' methods, so that the cancer cells displaying these antigenic peptides will stimulate the immune system to produce more cytotoxic T cells, resulting in cytotoxic T cell mediated killing of cancer cells, as recited in Applicants' claims. Hence, peptide antigens are selected for Applicants' claimed methods that can stimulate T cells to produce cytotoxic T cell mediated cell killing. Accordingly, the Examiner's concerns about the generation of a class II MHC cytotoxic T cell response and any concerns about the scope of the antigenic peptide to be employed, are unfounded.

The Examiner further maintains that factors not disclosed in the specification are critical to the functionality of the claimed method, citing the declaration of inventor Hogset, which according to the Examiner, suggests that toxic molecules may be used or generated in the methods. However, the language of Applicants' claims guides one of skill in the art to select an appropriate photochemical treatment procedure and an appropriate antigenic peptide so that the toxicity issue is obviated. Thus, claims 2 and 37 recite that the photosensitizing agent is selected from the group consisting of a porphyrin, phthalocyanine and a chlorine (i.e., three types of agents). These claims also require that the irradiation step release the peptide into the cytosol of cell without killing the cell.

Clearly, determination of the amount of light to achieve the results recited in the claims requires only routine experimentation by one of average skill in the art. Methods and reagents for photochemical treatment of cells have been available to those of skill in the art for a number of years. Methods for determining whether a cell is dead or viable are also available to those of even minimal skill in the art. Therefore, any one of average skill in the art can readily ascertain the conditions required and select one of the three types of photosensitizing agents recited in Applicants' claims to successfully expose a cell to light without killing it.

With respect to the toxicity of the antigenic peptide to be employed in the methods, Applicants submit that the Examiner is setting the bar very low for the skilled person's capabilities if this objection is to be given any weight. In essence, the Examiner asserts that the skilled person would not realize whether he or she should select a toxic or non-toxic molecule. Clearly, if the skilled artisan is using the methods of the invention, which involve presentation of an antigenic peptide on the surface of a live cell, a non-toxic peptide should be employed. Otherwise, the toxicity of the toxic molecule would kill the cell and no surface presentation could occur. If the toxicity of a molecule is unknown, appropriate experiments would be conducted to ensure that toxicity was not a problem. Even a lay person would be appreciative of the need not to administer potentially toxic agents to patients. No one of even minimal training in the art could be sufficiently confused to utilize a toxic molecule for the purposes of cell surface presentation. Moreover, because the treatment is for cancer, even those with minimal training would recognize that a cancer-related antigenic peptide should be employed.

Applicants submit that the specification clearly enables the subject matter of the claims and respectfully request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

§ 102 Rejection of the Claims

Claims 2, 4, 8-10, 28-37, and newly added claims 39 and 40 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by WO 96/07432 (IDS). The Examiner alleges that WO 96/07432 teaches a method of internalizing molecules, including non-toxic molecules such as sugars, proteins and peptides that will be presented on the on the surface of a cell and that the functionality of the majority of the cells will be maintained after such internalization (citing page 2 and the Abstract of WO 96/07432).

However, Applicants claims are directed to methods involving cancer cells. The teachings of WO 96/07432 with respect to cancer cells are significantly more limited than the Examiner has stated. For example, WO 96/07432 emphasizes that for cancer treatment "enhanced cytotoxic effects" and "enhanced specificity of the toxin" employed are the desirable outcome of using the methods described by WO 96/07432 (see WO 96/07432 at page 7, lines 14-18). Moreover, each of the twelve Examples of the WO 96/07432 disclosure illustrates internalization of toxins. Accordingly, although WO 96/07432 speculates that some non-toxic

molecules may be internalized into non-cancerous cells, when WO 96/07432 describes cancer treatment it is limited to use of toxins.

The passage to which the Examiner refers concerns the maintenance of functionality despite the photochemical internalization method and does not take into account any subsequent effect from the introduced molecule. Thus, page 3, first paragraph, elaborates that the photosensitizer is activated so that only the "endosomal, lysosomal or other cellular compartment membranes are ruptured and the molecules released in the cytosol without the cell losing its functionality by the action of the photoactivated compound and possible action of the endosomal/lysosomal content." Thus, this retention of functionality is concerned with limiting the extent of photochemical activation to avoid destruction of the cell. This does not also imply that regardless of the molecule that is transferred into the cell the cell should remain functional. Therefore, in terms of the cancer treatment described by WO 96/07432, the photochemical internalization step may not lead to a loss of functionality of the cell, but the toxins that are internalized will lead to a loss of functionality.

The only teaching by WO 96/07432 in relation to cancer cells is that cell death is to be achieved by the introduced molecule. To maintain the functionality of the cells even after the molecule has been introduced would be counterintuitive in view of the teachings of WO 96/07432 because the method of WO 96/07432 is aimed at therapy. If cell death is achieved, cell surface presentation cannot occur because there are no viable cells on which it can occur.

Moreover, WO 96/07432 utterly fails to disclose any expression or presentation of antigenic peptides on the cell surface. The present invention for the first time provides motivation for maintaining the cells' functionality even after the internalized molecule has been released into the cytosol as it allows the cells to present antigen and for that antigen to be targeted by cytotoxic T cells to then achieve death of the cancer cells. In contrast in WO96/07432, the authors were not aware that surface presentation could be achieved with photochemical internalization, and the methods advocated therein relied on achieving cell death with the introduced molecule, i.e. the molecule introduced is toxic thus leading to cell death.

Withdrawal of this rejection under 35 U.S.C. § 102(b), is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's representative at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or deficiencies, or credit any overpayments to Deposit Account No. 19-0743.

Respectfully submitted,

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Date January 15, 2010

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 15TH day of January, 2010.

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Signature